

We claim:

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1. A virus genome that encodes an RNA-dependent polymerase, the genome being modified to produce an attenuated virus, the genome further comprising at least one *pol* gene modification, which results in a decreased reversion rate from attenuated virus to non-attenuated virus as compared with an equivalent virus genome without the *pol* gene modification.
 2. The virus genome of claim 1, wherein the RNA-dependent polymerase is an RNA polymerase.
 3. The virus genome of claim 2, wherein the virus genome is an enterovirus genome.
 4. The virus genome of claim 3, wherein the enterovirus is selected from the group consisting of coxsackievirus, poliovirus polio-like virus and echovirus.
 5. The virus genome of claim 4, wherein the virus is coxsackievirus B, serotype 3 (CVB3).
 6. The virus genome of claim 1, wherein the RNA-dependent polymerase is a DNA polymerase.
 7. The virus genome of claim 6, from a virus selected from the group consisting of HIV, HTLV, ASLV, FeLV, BIV, and EIAV.
 - ~~8. The virus genome of claim 1, wherein the decreased reversion rate is caused by a decrease in rate of polymerase activity.~~

- 22 -

9. The virus genome of claim 1, wherein *pol* gene modification results in a polymerase having increased fidelity as compared with a polymerase from a virus genome that does not comprise the *pol* gene modification.

10. The virus genome of claim 1, wherein the *pol* gene modification comprises a mutation resulting in an alteration of the RNA polymerase active site.

11. The virus genome of claim 1, having a reversion rate at least two-fold decreased as compared with an equivalent virus without the *pol* gene modification.

12. A viral vector for delivering a heterologous nucleic acid to a target cell, tissue or organ, comprising the virus genome of claim 1, said genome further comprising at least one cloning site for insertion of an expressible heterologous nucleic acid.

13. The vector of claim 12, comprising an expressible heterologous nucleic acid encoding an antigenic molecule.

14. The vector of claim 12, comprising an expressible heterologous nucleic acid encoding a biologically active molecule.

15. A live, attenuated viral vaccine comprising the virus genome of claim 1.

16. A coxsackievirus 3B (CVB3) genome, modified to produce an attenuated virus, the genome further comprising at least one *pol* gene modification, which results in a decreased reversion rate from the

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Sub-B17

- 23 -

attenuated virus to non-attenuated virus as compared with an equivalent virus genome without the *pol* gene modification.

5 17. The CVB3 genome of claim 16, wherein the decreased reversion rate is caused by a decrease in rate of polymerase activity.

10 18. The CVB3 genome of claim 16, wherein *pol* gene modification results in a polymerase having increased fidelity as compared with a polymerase from a CVB3 genome that does not comprise the *pol* gene modification.

15 19. The CVB3 genome of claim 16, wherein the *pol* gene modification comprises a mutation resulting in an alteration of the RNA polymerase active site.

20 20. The CVB3 genome of claim 19, wherein the *pol* gene modification comprises a mutation at a position on the genome encoding glycine 328.

25 21. The CVB3 genome of claim 20, wherein the mutation results in a change in glycine 328 to cysteine or alanine.

30 22. The CVB3 genome of claim 16, wherein the modification to produce an attenuated virus comprises altering a transcription regulatory region of the genome.

35 23. The CVB3 genome of claim 22, having its 5' untranslated region replaced with a 5' untranslated region from a heterologous genome.

- 24 -

24. The CVB3 genome of claim 22, wherein the genome is modified by changing U to C or G, or C to G, at nucleotide position 234 of the genome.

5 25. A viral vector for delivering a heterologous nucleic acid to a target cell, tissue or organ, comprising the virus genome of claim 16, said genome further comprising at least one cloning site for insertion of an expressible heterologous nucleic acid.

10 26. The vector of claim 25, comprising an expressible heterologous nucleic acid encoding an antigenic molecule.

15 27. The vector of claim 25, comprising an expressible heterologous nucleic acid encoding a biologically active molecule.

20 28. The vector of claim 25, wherein the cloning site is positioned between a coding sequence for a capsid protein and a coding sequence for viral protease.

25 29. The vector of claim 25, wherein the cloning site is positioned at the start of the genome's open reading frame, such that the inserted expressible heterologous DNA comprises a translation start codon and a 3' sequence recognized by a viral protease.

30 30. A live, attenuated coxsackievirus vaccine comprising the CVB3 genome of claim 16.